```
FILE 'REGISTRY' ENTERED AT 09:18:49 ON 04 NOV 2002

=> S HISTIDINE AMMONIA LYASE/CN
L1             0 HISTIDINE AMMONIA LYASE/CN

=> S HISTIDASE/CN
L2             1 HISTIDASE/CN

=> D

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   9013-75-6  REGISTRY
CN   Ammonia-lyase, histidine (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   E.C. 4.3.1.3
CN     ***Histidase***
CN   Histidinase
CN   Histidine .alpha.-deaminase
CN   Histidine ammonia-lyase
CN   Histidine deaminase
CN   L-Histidase
CN   L-Histidine ammonia-lyase
MF   Unspecified
CI   MAN
LC   STN Files:   AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,
       CAPLUS, CHEMCATS, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA,
       NAPRALERT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             551 REFERENCES IN FILE CA (1962 TO DATE)
               4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             551 REFERENCES IN FILE CAPLUS (1962 TO DATE)


FILE 'CAPLUS' ENTERED AT 09:19:48 ON 04 NOV 2002

=> S HISTIDINE AMMONIA LYASE;S HISTIDASE;S L2;S L3,L4,L5
         59502 HISTIDINE
          1856 HISTIDINES
         60053 HISTIDINE
                 (HISTIDINE OR HISTIDINES)
        153575 AMMONIA
           113 AMMONIAS
        153633 AMMONIA
                 (AMMONIA OR AMMONIAS)
         13716 LYASE
          1341 LYASES
         14082 LYASE
                 (LYASE OR LYASES)
L3         243 HISTIDINE AMMONIA LYASE
                 (HISTIDINE(W)AMMONIA(W)LYASE)


           546 HISTIDASE
            15 HISTIDASES
L4         547 HISTIDASE
                 (HISTIDASE OR HISTIDASES)


L5         552 L2


L6         759 (L3 OR L4 OR L5)

=> S CORYNEBACTERIACEAE;S CORYNEBACTERIA
L7          43 CORYNEBACTERIACEAE


L8         544 CORYNEBACTERIA

=> S HISTIDINOL
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      545 HISTIDINOL
        1 HISTIDINOLS
L9    545 HISTIDINOL
          (HISTIDINOL OR HISTIDINOLS)

=> S L6 AND L9
L10     8 L6 AND L9

=> D 1-8 CBIB ABS
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L10 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS

2001:781102 Document No. 135:328746 Cloning, overexpression and therapeutic uses of bioactive ***histidine*** ***ammonia*** ***lyase*** from Corynebacteriaceae. Sethuraman, Natarajan; Roberts, Joseph; MaCallister, Thomas (ME Medical Enzymes A.-G., Switz.). PCT Int. Appl. WO 2001079469 A2 20011025, 98 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US12053 20010413. PRIORITY: US 2000-PV197770 20000414.

AB ***Histidine*** ***ammonia*** ***lyase*** isolated from Corynebacteriaceae can decrease serum histidine levels, induce accumulation of urocanic acid, and is not inhibited by L-***histidinol*** . A full-length gene and encoded amino acid sequences of ***histidine*** ***ammonia*** ***lyase*** from Corynebacteriaceae are disclosed. As a result, ***histidine*** ***ammonia*** ***lyases*** similar to the one isolated from Corynebacteriaceae are uniquely suitable for combination therapy with L-***histidinol*** to treat histidine- and/or histamine-dependent pathologies, for example, infectious viruses, such as human Respiratory Syncytial Virus (RSV), Herpes Simplex Virus (HSV), and Human Immunodeficiency Virus (HIV), as well as cancers.

L10 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS

2001:634532 Document No. 136:242628 Nucleotide sequence and predicted functions of the entire Sinorhizobium meliloti pSymA megaplasmid. Barnett, Melanie J.; Fisher, Robert F.; Jones, Ted; Komp, Caridad; Abola, A. Pia; Barloy-Hubler, Frederique; Bowser, Leah; Capela, Delphine; Galibert, Francis; Gouzy, Jerome; Gurjal, Mani; Hong, Andrea; Huizar, Lucas; Hyman, Richard W.; Kahn, Daniel; Kahn, Michael L.; Kalman, Sue; Keating, David H.; Palm, Curtis; Peck, Melicent C.; Surzycki, Raymond; Wells, Derek H.; Yeh, Kuo-Chen; Davis, Ronald W.; Federspiel, Nancy A.; Long, Sharon R. (Department of Biological Sciences, Stanford University, Stanford, CA, 94305, USA). Proceedings of the National Academy of Sciences of the United States of America, 98(17), 9883-9888 (English) 2001. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB The symbiotic nitrogen-fixing soil bacterium Sinorhizobium meliloti contains three replicons: pSymA, pSymB, and the chromosome. We report here the complete 1354,226-nt sequence of pSymA. In addn. to a large fraction of the genes known to be specifically involved in symbiosis, pSymA contains genes likely to be involved in nitrogen and carbon metab., transport, stress, and resistance responses, and other functions that give S. meliloti an advantage in its specialized niche.

L10 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS

2001:634531 Document No. 136:258038 Analysis of the chromosome sequence of the legume symbiont Sinorhizobium meliloti strain 1021. Capela, Delphine; Barloy-Hubler, Frederique; Gouzy, Jerome; Bothe, Gordana; Ampe, Frederic; Batut, Jacques; Boistard, Pierre; Becker, Anke; Boutry, Marc; Cadieu, Edouard; Dreano, Stephane; Gloux, Stephanie; Godrie, Therese; Goffeau, Andre; Kahn, Daniel; Kiss, Erno; Lelaure, Valerie; Masuy, David; Pohl, Thomas; Portetelle, Daniel; Puhler, Alfred; Purnelle, Benedicte; Ramsperger, Ulf; Renard, Clotilde; Thebault, Patricia; Vandenbol, Micheline; Weidner, Stefan; Galibert, Francis (Laboratoire de Biologie Moleculaire des Relations Plantes-Microorganismes, Unite Mixte de

Recherche (UMR) 215 Centre National de la Recherche Scientifique (CNRS), Institut National de la Recherche Agronomique, Chemin, Tolosan, F-31326, Fr.). Proceedings of the National Academy of Sciences of the United States of America, 98(17), 9877-9882 (English) 2001. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB Sinorhizobium meliloti is an .alpha.-proteobacterium that forms agronomically important N2-fixing root nodules in legumes. We report here the complete sequence of the largest constituent of its genome, a 62.7% GC-rich 3654,135-bp circular chromosome. Annotation allowed assignment of a function to 59% of the 3341 predicted protein-coding ORFs, the rest exhibiting partial, weak, or no similarity with any known sequence. Unexpectedly, the level of reiteration within this replicon is low, with only two genes duplicated with more than 90% nucleotide sequence identity, transposon elements accounting for 2.2% of the sequence, and a few hundred short repeated palindromic motifs (RIME1, RIME2, and C) widespread over the chromosome. Three regions with a significantly lower GC content are most likely of external origin. Detailed annotation revealed that this replicon contains all housekeeping genes except two essential genes that are located on pSymB. Amino acid/peptide transport and degrdn. and sugar metab. appear as two major features of the S. meliloti chromosome. The presence in this replicon of a large no. of nucleotide cyclases with a peculiar structure, as well as of genes homologous to virulence determinants of animal and plant pathogens, opens perspectives in the study of this bacterium both as a free-living soil microorganism and as a plant symbiont.

L10 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS

1993:534183 Document No. 119:134183 Inactivation of ***histidine*** ***ammonia*** - ***lyase*** from Streptomyces griseus by dicarbonyl reagents. White, Peter J.; Kendrick, Kathleen E. (Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210, USA). Biochimica et Biophysica Acta, 1163(3), 273-9 (English) 1993. CODEN: BBACAQ. ISSN: 0006-3002.

AB ***Histidine*** ***ammonia*** - ***lyase*** from Streptomyces griseus was inactivated by methylglyoxal and phenylglyoxal, dicarbonyl reagents known to react specifically with arginyl residues in proteins. The inactivation showed pseudo-first-order kinetics and could be prevented by protection with ***histidinol*** phosphate, a competitive inhibitor of ***histidine*** ***ammonia*** - ***lyase*** . Anal. of the amino acid compn. of ***histidine*** ***ammonia*** - ***lyase***. after treatment with phenylglyoxal, together with the kinetics of inactivation, suggested that inactivation was a consequence of specific reaction with one or more essential arginyl residues at or near the active site of the enzyme.

L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS

1993:250244 Document No. 118:250244 ***Histidine*** ***ammonia*** - ***lyase*** from Streptomyces griseus. Wu, Pen Chaur; Kroening, Terry A.; White, Peter J.; Kendrick, Kathleen E. (Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210, USA). Gene, 115(1-2), 19-25 (English) 1992. CODEN: GENED6. ISSN: 0378-1119.

AB ***Histidine*** ***ammonia*** - ***lyase*** (***histidase*** ; HutH) has been purified to homogeneity from S. griseus and the N-terminal amino acid (aa) sequence used to clone the ***histidase*** -encoding structural gene, hutH. The purified enzyme shows typical satn. kinetics and is inhibited competitively by D-histidine and ***histidinol*** phosphate. High concns. of K.cntdot.cyanide inactivate HutH unless the enzyme is protected by the substrate or ***histidinol*** phosphate. On the basis of the nucleotide sequence, the hutH structural gene would encode a protein of 53 kDa with an N terminus identical to that detd. for the purified enzyme. Immediately upstream from hutH is a region that strongly resembles a class of Streptomyces promoters active during vegetative growth; however, there is no obvious ribosome-binding site adjacent to the hutH translation start codon. The deduced aa sequence of an upstream partial open reading frame shows no similarity with other proteins, including HutP of Bacillus subtilis and HutU of Pseudomonas putida. Promoter-probe anal. indicates that promoter activity maps within the DNA surrounding the hutH start codon. Pairwise comparisons of the primary structures of bacterial and mammalian ***histidases*** , together with the unique kinetic properties and gene organization, suggest that streptomycete ***histidase*** may represent a distinct family of ***histidases*** .

L10 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
1993:186719 Document No. 118:186719 Purification of ***histidase*** from Streptomyces griseus and nucleotide sequence of the hutH structural gene. Wu, Pen Chaur; Kroening, Terry A.; White, Peter J.; Kendrick, Kathleen E. (Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA). Journal of Bacteriology, 174(5), 1647-55 (English) 1992. CODEN: JOBAAY. ISSN: 0021-9193.

AB ***Histidine*** ***ammonia*** - ***lyase*** (***histidase***) was purified to homogeneity from vegetative mycelia of S. griseus. The enzyme was specific for L-histidine and showed no activity against the substrate analog, D-histidine. ***Histidinol*** phosphate was a potent competitive inhibitor. ***Histidase*** displayed satn. kinetics with no detectable sigmoidal response. Neither thiol reagents nor a variety of divalent cations had any effect on the activity of the purified enzyme. High concns. of potassium cyanide inactivated histdase in the absence of its substrate or ***histidinol*** phosphate, suggesting that, as in other ***histidases*** , dehydroalanine plays an important role in catalysis. The N-terminal amino acid sequence of ***histidase*** was used to construct a mixed oligonucleotide probe to identify and clone the ***histidase*** structural gene, hutH, from genomic DNA of the wild-type strain of S. griseus. The cloned DNA restored the ability of a ***histidase*** structural gene mutant to grow on L-histidine as the sole nitrogen source. The deduced amino acid sequence of hutH shows significant relatedness with ***histidase*** from bacteria and a mammal as well as phenylalanine ammonia-lyase from plants and fungi.

L10 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
1976:401633 Document No. 85:1633 ***Histidine*** ***ammonia*** - ***lyase*** from rat liver. Purification, properties, and inhibition by substrate analogs. Brand, Larry M.; Harper, Alfred E. (Coll. Agric. Life Sci., Univ. Wisconsin, Madison, Wis., USA). Biochemistry, 15(9), 1814-21 (English) 1976. CODEN: BICHAW.

AB ***Histidine*** ***ammonia*** - ***lyase*** (I) from rat liver was purified >250-fold to near homogeneity. Electrophoretic detns. indicated a native mol. wt. of .apprx.200,000. The enzyme had a pH optimum of .apprx.8.5. The min. Km for L-histidine was 0.5 mM at pH 9.0. The Km in the physiol. pH range was, however, >2.0 mM. D-.alpha.-hydrazinoimidazolylpropionic acid was a potent competitive inhibitor of liver I; the L enantiomer of this compd. was less effective in this regard. The enzyme was also inhibited competitively by L-histidine hydroxamate (Kis = 0.4 mM), and to a lesser extent by L-***histidinol*** , D-histidine, and glycine. Failure of a wide variety of other histidine analogues to inhibit the enzyme substantially indicates high specificity of the active site for L-histidine. No alternate substrates were identified for the enzyme. DL-.alpha.-hydrazinophenylpropionic acid, the .alpha.-hydrazino analog of phenylalanine, was a very potent competitive inhibitor of a mechanistically similar L-phenylalanine ammonia-lyase purified from Rhodotorula glutinis. The properties of I from rat liver differed significantly from those of the enzyme from Pseudomonas fluorescens, which has been studied most extensively to date.

L10 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
1965:76259 Document No. 62:76259 Original Reference No. 62:13537d-f Bursts of enzyme synthesis in the bacterial duplication cycle. Kuempel, Peter L.; Masters, Millicent; Pardee, Arthur B. (Princeton Univ., Princeton, NJ). Biochem. Biophys. Res. Commun., 18(5-6), 858-67 (English) 1965.

AB cf. CA 60, 13614a. Explorations were made of bursts of enzyme syntheses under normal growth conditions in CS 101-G-1, a guanine auxotroph of Escherichia coli, and in Bacillus subtilis to elucidate why enzyme-formation potential (defined as the max. ability for enzyme synthesis, such as should be obtained by complete derepression), while always present, is expressed only intermittently under normal growth conditions, and how it differs from the autogenous rate of enzyme synthesis (i.e., the amt. of enzyme elaborated/min. in a growing culture). A model was described to explain the results. Potential existed at all times for the synthesis of all enzymes examd. (alk. phosphatase, aspartic transcarbamylase, dihydroorotase, .beta.-galactosidase, ***histidase*** , ***histidinol*** dehydrogenase, tryptophanase), changing abruptly at

different times for each enzyme. Bursts of autogenous enzyme synthesis were also demonstrated, some enzymes being synthesized continuously, while others were not. Details were given of 1 of several explanations devised for these bursts of autogenous enzyme synthesis by employing a simple model of enzyme repression based on interactions of changing potentials, degrees of repression, and diln. of the system by growth.

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=> S (L7,L8) AND L6
L11          2 ((L7 OR L8)) AND L6

=> S L11 NOT L10
L12          1 L11 NOT L10

=> D CBIB ABS

L12  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
1979:551304  Document No. 91:151304  Biologic and antineoplastic effects of
     enzyme-mediated in vivo depletion of L-glutamine, L-tryptophan, and
     L-histidine.  Roberts, Joseph; Schmid, Franz A.; Rosenfeld, Henry J.
     (Sloan-Kettering Inst. Cancer Res., Rye, NY, 10580, USA).  Cancer Treat.
     Rep., 63(6), 1045-54 (English) 1979.  CODEN: CTRRDO.  ISSN: 0361-5960.
AB   Novel enzymes, capable of depleting L-glutamine  [56-85-9] plus
     L-asparagine  [70-47-3], L-tryptophan  [73-22-3], were purified from soil
     isolate organisms.  L-Glutaminase-L-asparaginase (I)  [39335-03-0] from
     Pseudomonas 7A demonstrated substantial antineoplastic activity against a
     variety of L-asparaginase-resistant leukemias (L1210, EARAD/1/AR, and
     C1498), an ascites tumor (Taper liver tumor), and solid tumors (B16
     melanoma and Walker 256 carcinosarcoma).  I from Pseudomonas 7A was
     considerably more potent antitumor agent than I from Acinetobacter .
     Tumors did not develop resistance to I as they do to Escherichia coli
     L-asparaginase (EC-2).  Resistance to EC-2 by EARAD/1 leukemia cells
     developed in treatment of 2 generations.  By contrast, after treatment of
     10 generations with I, EARAD/1 leukemia cells were just as sensitive to
     both L-glutaminase-L-asparaginase and EC-2 as the parent tumor.
     Combination therapy with I plus methotrexate  [59-05-2] or azaserine
     [115-02-6] appeared promising.  Indolyl-3-alkane .alpha.-hydroxylase
     [63363-76-8], which attacks the side chain of L-tryptophan, serotonin, and
     other 3-substituted indole compds., caused marked depletion of
     L-tryptophan and serotonin  [50-67-9] in body fluids and certain tissues.
     This enzyme exhibited significant antineoplastic activity against a
     variety of mouse tumors: Meth A sarcoma, Ehrlich carcinoma, and Taper
     liver tumor.  An L-  ***histidase***    [  ***9013-75-6***  ], which had
     near-optimal activity in the physiol. pH range and a Km of 1 mM, was
     isolated from a soil organism belonging to the  ***Corynebacteriaceae***
     .  The plasma half-life of this L-  ***histidase***  in mice was .apprx.8
     h.  Treatment of tumor-bearing mice with 500 IU L-  ***histidase***
     /kg/day maintained plasma L-histidine at unmeasurably low levels (<3
     nmol/mL) and resulted in inhibition of total packed cell vol. of the
     ascitic forms of Ehrlich carcinoma and Meth A sarcoma.

=> E ROBERTS J/AU
=> S E3
L13        180 "ROBERTS J"/AU

=> S L3
         59502 HISTIDINE
          1856 HISTIDINES
         60053 HISTIDINE
                 (HISTIDINE OR HISTIDINES)
        153575 AMMONIA
           113 AMMONIAS
        153633 AMMONIA
                 (AMMONIA OR AMMONIAS)
         13716 LYASE
          1341 LYASES
         14082 LYASE
                 (LYASE OR LYASES)
L14        243 HISTIDINE AMMONIA LYASE
                 (HISTIDINE(W)AMMONIA(W)LYASE)
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=> S SETHURAMAN/AU
L15             0 SETHURAMAN/AU

=> S MACALLISTER T/AU
L16             0 MACALLISTER T/AU

=> E SETHURAMAN N/AU
=> S E3,E4
                1 "SETHURAMAN N"/AU
                3 "SETHURAMAN NATARAJAN"/AU
L17             4 ("SETHURAMAN N"/AU OR "SETHURAMAN NATARAJAN"/AU)

=> E MACALLISTER T/AU
=> S E4,E5
                5 "MACALLISTER THOMAS"/AU
                3 "MACALLISTER THOMAS W"/AU
L18             8 ("MACALLISTER THOMAS"/AU OR "MACALLISTER THOMAS W"/AU)

=> S L13,L14,L17,L18
L19           432 (L13 OR L14 OR L17 OR L18)

=> S L19 AND L6
L20           243 L19 AND L6

=> S L20 AND (L7,L8)
L21             1 L20 AND ((L7 OR L8))

=> S L21 NOT (L10,L12)
L22             0 L21 NOT ((L10 OR L12))

=> S L20 AND L9
L23             7 L20 AND L9

=> S L23 NOT (L10,L12)
L24             0 L23 NOT ((L10 OR L12))
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